

Application No. 10/699,393  
Response Dated January 18, 2007  
Second Reply to Office Action of August 24, 2006

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### Amendments to the Specification

Please replace the paragraph on page 1, lines 6-7 with the following replacement paragraph:

The present application is a divisional application of, and claims benefit of U.S. Patent Application Serial No. 10/165,422, filed June 7, 2002, entitled "Antithrombotic thrombin variants," now issued as U.S. Pat. No. 6,706,512, which itself claims benefit of priority from U.S. Provisional Application Serial No. 60/297,089, filed June 8, 2001, ~~the disclosure of which is hereby incorporated herein in its entirety by reference.~~

Please replace the paragraph on page 7, lines 17-28 with the following replacement paragraph:

Fig. 1 illustrates the amino acid sequence of the thrombin variant W215A (SEQ ID NO:1). The substitution W215A is in bold. The amino acid numbering system herein is based on the Sadler numbering scheme. The A chain of thrombin is designated with "a" postscripts, as in T1a to R36a, while the B chain commences with I1 and extends to E259.

Fig. 2 illustrates the amino acid sequence of the thrombin variant W215A B-chain (SEQ ID NO:2). The amino acid numbering system herein is based on the Sadler numbering scheme. The B chain commences with I1 and extends to E259.

Fig. 3 illustrates the amino acid sequence of the thrombin variant W215A/E217A (SEQ ID NO:3). The amino acid substitutions W215A and E217A are in bold. The amino acid numbering system herein is based on the Sadler numbering scheme. The A chain of thrombin is designated with "a" postscripts, as in T1a to R36a, while the B chain commences with I1 and extends to E259.

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Fig. 4 illustrates the amino acid sequence of the thrombin variant W215A/E217A (WE) B-chain (SEQ ID NO:4). The amino acid numbering system herein is based on the Sadler numbering scheme. The B chain commences with I1 and extends to E259.